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Kevin P Francis

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EXAMINER
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SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 06/04/2002

17

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/657,289

Applicant(s)

FRANCIS ET AL.

Examiner

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 28 March 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-8, 21, 22, 24-29, 34-36, 49, 56, 58, 60, 62, 64 and 68-86 is/are pending in the application.
- 4a) Of the above claim(s) 60 and 83-86 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8, 21, 22, 24-29, 34-36, 49, 56, 58, 62, 64 and 68-82 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 September 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9, 11, 12. 6) ☐ Other: \_\_\_\_\_

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### **DETAILED ACTION**

The amendment filed March 28, 2002 (Paper No. 16) canceling claims 9-20, 23, 30-33, 37-48, 50-55, 57, 59, 61, 63 and 65-67, amending claims 1-3, 5-8, 21, 22, 24-28, 36, 49, 58, 60, 62 and 64 and adding claims 68-86 has been entered.

Claims 1-8, 21, 22, 24-29, 34-36, 49, 56, 58, 60, 62, 64 and 68-86 are pending.

### ***Election/Restriction***

Applicant's election with traverse of Group I in Paper No. 16 is acknowledged. The traversal is on the ground(s) that "the inclusion of claims 60 and 61 in Group III is inappropriate as those claims are not directed to a transgenic animal, the claims are directed to a Gram-positive bacteria comprising a luciferase expression cassette (according to claim 1) wherein the Gram-positive bacteria is introduced into a whole animal. Accordingly, applicants submit that claims 60 and 61 are properly grouped with the claims of Group I" (paragraph bridging pages 2 and 3). This is not found persuasive because while claims 60 and 61 may be restricted from Group III, they should be restricted from Group I as well. Group I includes a method of screening an analyte in bacteria. A method of screening an analyte in a living animal of claims 60 and 61 and the method of Group I are differently classified (classes 435/252.3; 436/2 and class 424/9.1, respectively). Further, the methods of Group I and of claims 60 and

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61 are materially different as employing bacteria and living animals and requiring different protocols, chemicals and having different utility.

The requirement is still deemed proper and is therefore made FINAL.

Claim 61 is canceled in Paper No. 16, *supra*. Claim 60 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group III, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 16.

Newly submitted claims 83-86 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: set forth above with regard to claims 60 and 61.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 83-86 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-8, 21, 22, 24-29, 34-36, 49, 56, 58, 62, 64 and 68-83 are under consideration.

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***Specification***

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

See, for example, page 15, line 3.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-8, 21, 22, 24-28, 34-36, 49, 56, 58, 62, 64 and 68-83 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 5-8, 21, 22, 24-28, 34-36, 49, 56, 58, 62, 64 and 68-83 comprise polynucleotides encoding "lux" genes. The specification defines "lux" genes as "prokaryotic genes associated with luciferase and photon emission" (page 18, lines 22-23). Thus, a genus of any "lux" gene encompasses both naturally occurring in any prokaryote and man made or mutated genes.

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The claims are not limited to *lux* genes from Gram-negative bacterium homologous to *lux* genes from *Photorhabdus luminescens*. The specification does not contain any disclosure of the structure and function of all DNA sequences that encode a *lux* polypeptide or portions thereof. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many structurally and functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus, a DNA encoding *lux* gene products from Gram-negative bacterium *Photorhabdus* (*Xenorhabdus*) *luminescens*. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the "functionality" of encoding a *lux* polypeptide and fails to provide any structure: function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claim 62 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a strain of *S. aureus* comprising a plasmid DNA

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comprising *P. luminescens lux* operon (*lux ABCDE*) and SEQ ID NO:1 at least seven nucleotides upstream of each start codon, does not reasonably provide enablement for any Gram-positive bacteria comprising *lux A*, *lux B*, *lux C*, *lux D* and *lux E* wherein about  $1 \times 10^6$  cells produce at least about  $1 \times 10^4$  DNA Relative Lights Units at about 37° C. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Factors to be in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification teaches that "none of the bioluminescent Gram-positive bacteria which have been published to date produce enough light" (page 2, lines 22-23). The state of the art is such that it is a priori unpredictable how the cassette should be constructed in order to have the requisite characteristics. The specification teaches a specific cassette with a specific sequence that when introduced in *S. aureus* provides the desired result. The scope of the claims is not commensurate with the enablement

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provided by the disclosure with regard to the extremely large number of constructs broadly encompassed by the claims.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen a large number of possible combinations .

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of possible nucleotide arrangements of a cassette comprising *lux A*, *lux B*, *lux C*, *lux D* and *lux E* and any other nucleotide sequences. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a make up of a cassette that would impart the requisite properties to any Gram-positive bacterium is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21, with dependent claims 22, 24-29, 76-82 is rejected under 35 U.S.C.

112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites "*luc*" gene that is not defined in the specification.



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Claim 82 recites "said substrate is (I) aldehyde and is provided as a vapor, and (ii) a substrate for the *luc* gene product (emphasis added). It appears that some words are missing.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 4-8, 34-36, 49, 56, 58, 64 and 75 are rejected under 35 U.S.C.

103(a) as being unpatentable over Meighen in view of Vellanoweth et al.

Meighen et al. (form PTO-1449 filed October 16, 2001, reference AR-1) teach organization and function of the *lux* genes in Gram-negative bacteria and their expression in Gram-negative bacteria. They teach that the luciferase genes (*luxAB*) are flanked by genes involved in synthesis of its fatty aldehyde substrate (*luxCDE*) (page 122).

Vellanoweth et al. teach that Gram-positive ribosomes are unable to translate mRNAs containing weak Gram-negative RBSs. They teach that spacing between the

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RBS and the start codon on Gram-positive mRNAs should ideally be 7 to 10 nucleotides.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use Gram-positive RBS in cassettes comprising the entire *lux* operon and intended for transforming Gram-positive bacteria as taught by Vellanoweth et al.

Claims 21, 24-29 and 70-74 and 76-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schauer in view of Vellanoweth et al.

Schauer teaches a fusion gene comprising *luxA* and *luxB* and firefly luc gene. organization and function of the *lux* genes in Gram-negative bacteria. They teach that the luciferase genes (*luxAB*) are flanked by fatty acid reductase genes (*luxCDE*) (page 122.

Vellanoweth et al. teach that Gram-positive ribosomes are unable to translate mRNAs containing weak Gram-negative RBSs. They teach that spacing between the RBS and the start codon on Gram-positive mRNAs should ideally be 7 to 10 nucleotides.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use Gram-positive RBS in cassettes comprising *luxAB* and luc

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genes and intended for transforming Gram-positive bacteria as taught by Vellanoweth et al.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schauer in view of Vellanoweth et al. and further in view of Meighen et al.

The teachings of Schauer, Vellanoweth et al and Meighen et al are outlined above.

In order to avoid addition of an exogenous aldehyde, it would have been obvious to one of ordinary skill in the art at the time the invention was made to express the lux genes encoding both the luciferase and the substrate using genes taught by Meighen et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

Elizabeth Slobodyansky, PhD  
Primary Examiner